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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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WILMERHALE/BOSTON
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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

NOTIFICATION DATE	DELIVERY MODE
12/09/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/576,981	ASHDOWN, MARTIN LEONARD	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-66 and 72-75* is/are pending in the application.

4a) Of the above claim(s) *48, 52-57, and 63-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-47,49-51,58-62,66 and 72-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 April 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 lists*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 45-66 and 72-75 are pending in the application.

Election/Restrictions

2. Applicant's election with traverse of Group I, and the species wherein f) an immune system marker is monitored, i) the disease is a cancer, and A) the agent to be administered inhibits the production of regulator cells, in the reply filed on July 10, 2008 is acknowledged. The traversal is on the ground(s) that the cited WO reference deals with resetting of an immune system, whereas the present claims are drawn to methods involving analyzing effector/regulator cell cycling.

This is not found persuasive because the portions of the reference cited in support for the finding that the present claims lack a common special technical feature (i.e. claims 1, 2, and 10) make no mention of resetting of an immune system, but indicate that the timing of administration of an agent to treat a disease is based upon an analysis of the cycling of effector cells. As the present claims are also directed to such timing of agents to treat a disease, the Applicant's arguments are not found persuasive.

Moreover, while the Applicant asserts that the present application, in contrast to the cited reference, is based upon the "surprising finding that the immune system is constantly cycling in disease states such as cancer," it is also noted that there is nothing in the independent claims in the application to distinguish between the methods of the present application and the cited art. I.e., both the prior art and independent claim 1 are directed to timing the administration of an anti-proliferative drug to a subject based on timing determined through monitoring an immune

system marker. Thus, regardless of the focus of the specifications of the present application and the prior art, the present claims read on the methods described in the prior art. Applicant's arguments are therefore not found persuasive.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 48, 52-57, and 63-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions or species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 10, 2008.

4. Claims 45-47, 49-51, 58-62, 66, and 72-75 are under consideration.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on March 26, 2007 and October 9, 2008 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements been considered by the examiner.

It is noted that the foreign patent documents in the October 2008 IDS are duplicative of references cited in the March 2007 IDS. These references have therefore been crossed out in the later IDS.

Specification

6. The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable

code. See e.g., page 30, line 19. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 45-47, 49-51, 58-62, 72-75 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 2003/068257 (WO'257- of record in the March 2007 IDS). These claims are drawn to methods for the treatment of a disease (esp. cancer) through timing the administration of an anti-proliferative drug (i.e. a drug that inhibits production of regulator cells) through the monitoring of an immune system marker, such as an acute phase inflammatory marker (e.g. C-reactive protein or CRP). The claims indicate that the agent is preferably administered between when the levels of the marker have peaked, and before they begin to rise in the next cycle. Additional claims require that the patient is monitored for at least 21 days at intervals of at least every 3 days (i.e. every 3 days or less- see. page 7, lines 2-28). Claim 61 requires that the patient has not been exposed to a treatment for at least 21 days.

The WO'257 reference teaches such a method. For example, claim 1 of the reference describes a method of treating cancer involving the administration of an agent that inhibits the production of regulator cells. The reference indicates that the agent is administered based on

fluctuations in the levels of CRP, and in particular, when the levels of the protein begin to decrease (i.e. after peak is achieved, and before the levels begin to rise again). The reference teaches examples wherein the monitoring is performed for at least 1 month (i.e. at least 21 days), and preferable occurs every 24 hours (i.e. at least every 3 days). Page 18, Example 4. Page 18 and claim 25 of the reference indicate that the method may be applied to human subjects.

As indicated above, claim 61 is directed to the method described above, wherein the subject is not exposed to a treatment for the disease for at least 21 days. The subject of claim 1 is a subject being monitored for the immune system marker. Thus, claim 31 is indicating that the patient is monitored for the immune system marker at a time period at least 21 days after any treatment has been applied to the patient.

The method of claim 1 in WO'257 involves a preliminary step of "reducing tumor load in the subject." However, the reference is silent as to the time period between the tumor load reduction therapy and the administration of the agent. On page 18 of the reference, an Example is provided indicating that monitoring of the patient for CRP levels (to determine when the agent inhibit regulator cell production should be administered) should continue for at least one month (an average of about 30 days). Thus, the reference teaches a method wherein the patient is monitored for an immune system marker for a period at least 21 days after therapy (i.e. a period where the patient has not been exposed to therapy for at least 21 days).

The reference therefore anticipates the indicated claims.

9. Claims 45, 47, 49, 50, 58, 60, 62, 66, and 72-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Child et al. (Cancer 45:318-26). These claims are generally drawn to

methods comprising monitoring a patient, esp. patients with cancer, or samples therefrom, for an immune system marker, such as a acute phase inflammatory marker (e.g. CRP). Claim 66 reads on a kit comprising a reagent for monitoring an immune system marker.

Child teaches the monitoring of patients with Hodgkin's disease or non-Hodgkin's lymphoma (types of cancers) for the levels of CRP in patient serum. See e.g., Figures 1, 4, and 6. The reference teaches the use of antisera against the proteins for the analysis. Page 319 (section titled "Serum proteins"). Thus, the reference teaches the methods and compositions of the claims.

While the reference does not indicate that CRP is monitored to determine timing of the administration of an agent to the patients, this is an intended use of the methods and compositions of the indicated claims. See, MPEP 2111.02 II. In the present case, the claims are drawn to methods for analyzing effector cell and/or regulator cell cycling to determine when an agent should be administered to a patent suffering from a disease characterized by the production of regulator cells, the method comprising monitoring the patient, or sample obtained therefrom, for… an immune system marker." The teachings of the specification and claims indicate that cancers are representatives of the indicated diseases, and that CRP is an example of the immune system markers. However, the claims do not require that the agent is actually administered. Thus, the claims read on methods for monitoring levels of CRP in cancer patients. Because Child teaches such methods, the claims are anticipated by the reference.

10. Claims 45-47, 49, 60, and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Little et al. (Curr Opin Oncol 12:438-44). These claims read on methods for the treatment of a

disease, such as a cancer, comprising administering an agent to treat the disease based on the monitoring of one of the markers of claim 45. Little teaches a method for the treatment of an AIDS related cancer (HIV-associated non-Hodgkin's lymphoma) comprising the administration of antiproliferative agent (i.e. a combination of such agents known as EPOCH) based on the count of CD4 cells in the patient (which includes a count of CD4 effector and regulator cells). See, page 441, right column. The reference therefore anticipates the indicated claims.

11. Claim 66 is rejected under 35 U.S.C. 102(b) as being anticipated by Eda et al. (J Clin Lab Anal 12:137-44- of record in the March 2007 IDS). This claim is drawn to a kit comprising a reagent for monitoring for an immune system marker. The application indicates that an example of such a marker is the protein C-reactive protein (CRP). See, page 4. Eda teaches an assay for CRP. In particular, the reference teaches the use of reagents for use in detecting the protein. Abstract, page 138. Because the claimed kit comprises only these reagents, and as the reference teaches the reagents, the reference anticipates the claim.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 45-47, 49-51, 58-62, and 72-75 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 26-28, 31-32, 35, 36-38, and 42-47 of copending Application No. 10/503794. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims are generic to the copending claims, and would be anticipated by them if applicable as prior art. It is noted that the copending claims require the use of a prior treatment which affects effector cells in the patient, whereas there is not such requirement in the present claims (and is in fact excluded to some extent by claim 61). However, with the exception of claim 61, there is nothing in the present claims to exclude the use of such a preliminary treatment.

With respect to claim 61, it is noted that the claim does not exclude the use of a prior treatment at all. Rather, the claim merely requires that the monitoring is conducted during a period preceded by at least 21 days in which not therapy is provided. The claims of the copending application provide no indication as to the term during which the patient is monitored after the treatment affecting the effector cells is applied. Thus, it would have been obvious to those of ordinary skill in the art to have continued the monitoring for as long as required until the correct time for administration of the agent to inhibit regulator cells had arrived. Such a period may or may not be after at least 21 days since the treatment was applied. Thus, it would have been obvious to those of ordinary skill in the art to have continued the monitoring for as long as

required, including during periods after 21 days from the time of the treatment. Claim 61 is therefore generic to at least some obvious embodiments of the copending claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 45-47, 49-51, 58-62, 72, and 74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6, 10-13, and 15 of copending Application No. 12/333/369. Although the conflicting claims are not identical, they are not patentably distinct from each other because the presently rejected claims are generic to the copending claims. Each set of claims deals with the treatment of a disease through the administration of an agent for the inhibition of production of regulator cells at a time point determined by monitoring the levels of an immune system marker, esp. an acute phage inflammatory marker such as CRP, and administering the agent where it appears that the regulator cells are being produced. The copending claims are limited to embodiments wherein the disease is a retroviral infection. The present claims are not so limited, but would encompass such embodiments, and thus be anticipated by them if applied as prior art. The obviousness type double patenting rejection is therefore appropriate.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648